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     FILE 'CAPLUS' ENTERED AT 11:53:04 ON 04 NOV 2002
                  E LEE KUEN/IN,AU
L1              36 S E4 OR E22-24
                  E MOONEY DAVID/IN,AU
L2             110 S E3-4 OR E8-9
L3              21 S L1 AND L2
L4           13946 S HYDROGEL
L5           73244 S POLYSACCHARIDE
L6          217398 S CROSSLINK?
L7          298929 S L4 OR L5 OR L6
L8              19 S L3 AND L7
L9              45 S (L1 OR L2) AND L7
L10             26 S L9 NOT L8
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L8 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:739817 CAPLUS
TITLE: Decoupling the dependence of rheological/mechanical properties of **hydrogels** from solids concentration
AUTHOR(S): Kong, Hyun-Joon; **Lee, Kuen Yong**; **Mooney, David J.**
CORPORATE SOURCE: Department of Biologic and Materials Sciences, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Polymer (2002), 43(23), 6239-6246
CODEN: POLMAG; ISSN: 0032-3861
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Hydrogels** are being increasingly used in medicine due to their potential to be delivered into the body in a minimally invasive manner (e.g. injection in soln. form) for subsequent gelation at the site of introduction. Both the flow properties of the soln. and mech. properties of the gels are crit. to their applications. However, both properties depend on the concn. of polymer, and simply increasing the concn. to improve the gel properties often leads to unacceptably high fluid viscosities. Thus, we hypothesized that **hydrogels** with a bimodal mol. wt. distribution (MWD) (i.e. a mixt. of high MW polymer and polymer tailored to have a lower MW but still able to participate in gel formation) would allow one to readily decouple the dependence of the two properties from the overall concn. This hypothesis was investigated using alginate **hydrogels**, and we found that increasing the concn. of alginate (Calginate) with high MW alginate from 2 to 5% raised the viscosity (.eta.) of soln. from 0.7 to 20 Pa s, while enhancing the shear modulus (G) from 25 to 50 kPa. In contrast, increasing Calginate of binary solns. at a wt. fraction of high MW alginate of 0.50 raised .eta. from 0.2 to only 3.6 Pa s, while enhancing G from 15 to 52 kPa. Strikingly, the low .eta. of binary solns. can be attributed to a significant decrease in phys. interactions between the chains, while strong gel strength could be attributed to an increased fraction of intermol. cross-links and stiffened mols. as compared to gels comprised of high MW alginates. This approach of adjusting the MWD of gel forming solns. to control the fluid and solid properties in an independent manner may be broadly utilized in designing other **hydrogels** and materials for a variety of applications.

L8 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:635677 CAPLUS
TITLE: Evaluation of Chain Stiffness of Partially Oxidized Polyguluronate
AUTHOR(S): **Lee, Kuen Yong**; Bouhadir, Kamal H.; **Mooney, David J.**
CORPORATE SOURCE: Departments of Biologic Materials Sciences and Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Biomacromolecules ACS ASAP
CODEN: BOMAF6; ISSN: 1525-7797
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The chain stiffness of macromols. is considered crit. in their design and applications. This study utilizes polyguluronate derived from alginate, a typical **polysaccharide** widely utilized in many biomedical applications, as a model macromol. to investigate how the chain stiffness can be tightly regulated by partial oxidn. Alginate has a backbone of inherently rigid .alpha.-L-guluronate (i.e., polyguluronate) and more flexible .beta.-D-mannuronate. The chain stiffness of the polyguluronate was specifically studied in this paper, as this component plays a crit. role in the formation of alginate **hydrogels** with divalent cations and is the dominant factor in detg. the chain stiffness of alginate. We have utilized size-exclusion chromatog., equipped with refractive index, viscosity, and light-scattering detectors, to det. the intrinsic viscosity and the wt.-av. mol. wt. of each fraction of samples. The chain stiffness of partially oxidized polyguluronate was then evaluated from the exponent of the Mark-Houwink equation and the persistence length. We have found that partial oxidn. can be used to

tightly regulate the steric hindrance and stiffness of the polyguluronate backbone. This approach to control the chain stiffness of inherently rigid **polysaccharides** by partial oxidn. may find many applications in biomedical utilization of these materials.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:545746 CAPLUS
TITLE: Controlled growth factor delivery by mechanical stimulation
AUTHOR(S): **Lee, Kuen Yong**; Peters, Martin C.; Anderson, Kenneth W.; **Mooney, David J.**
CORPORATE SOURCE: Dept. of Biologic & Materials Sciences, Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Materials Research Society Symposium Proceedings (2002), 711(Advanced Biomaterials: Characterization, Tissue Engineering and Complexity), 189-192
CODEN: MRSPDH; ISSN: 0272-9172
PUBLISHER: Materials Research Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Growth factor delivery using polymer matrixes is one exciting approach to replace or regenerate tissues. Most growth factor delivery systems, however, have been designed to operate under static conditions, regardless of dynamic environments in the body. Considering the dynamic environment of our body (e.g., bone, muscle, and blood vessel), mech. stimulation is an important signal that could be readily exploited. We hypothesize that polymer matrixes, which release growth factors in response to mech. stimulation, could provide a novel approach to engineer tissues in mech. stressed environments. We report here a model system, comprised of alginate **hydrogel** and vascular endothelial growth factor (VEGF), which upregulates the release of the growth factor in response to mech. stimulation and subsequently promotes granulation tissue formation in animals. This approach may find a no. of potential applications in tissue engineering, as well as in drug delivery.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:409132 CAPLUS
DOCUMENT NUMBER: 136:391057
TITLE: Drug release from polymer matrixes through mechanical stimulation
INVENTOR(S): **Lee, Kuen Yong**; Mooney, David J.
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002064559	A1	20020530	US 2001-983320	20011024
WO 2002078601	A2	20021010	WO 2001-US51603	20011026

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-243813P P 20001027
AB A method for drug delivery and polymer matrix suited to the method are disclosed. The polymer matrix has reversibly bound thereto a drug or combination of drugs, and is capable of releasing the drug or combination of drugs in response to mech. stimulation of the polymer matrix. According to the method of this invention, such a polymer matrix is

delivered to an in vivo locus, e.g., the site of a wound, trauma, etc., and mech. stimulation of said polymer matrix is effected in vivo, thereby releasing the drug or combination of drugs in the area of the in vivo locus. Alginate **hydrogels** were prepd. comprising Protanal, Trypan blue as a model drug, and CaSO4. One group of the sample **hydrogels** were subjected to mech. stimulation comprising three cycles of compression/relaxation by using a mech. tester. Release of the trypan blue drug from the compressed **hydrogels** increased steadily over the course of compression/relaxation cycles.

L8 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:610066 CAPLUS
DOCUMENT NUMBER: 135:308826
TITLE: Degradation of Partially Oxidized Alginate and Its Potential Application for Tissue Engineering
AUTHOR(S): Bouhadir, Kamal H.; **Lee, Kuen Yong**; Alsberg, Eben; Damm, Kelly L.; Anderson, Kenneth W.; **Mooney, David J.**
CORPORATE SOURCE: Departments of Biologic & Materials Sciences Chemical Engineering and Biomedical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Biotechnology Progress (2001), 17(5), 945-950
CODEN: BIPRET; ISSN: 8756-7938
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alginate has been widely used in a variety of biomedical applications including drug delivery and cell transplantation. However, alginate itself has a very slow degrdn. rate, and its gels degrade in an uncontrollable manner, releasing high mol. wt. strands that may have difficulty being cleared from the body. We hypothesized that the periodate oxidn. of alginate, which cleaves the carbon-carbon bond of the cis-diol group in the uronate residue and alters the chain conformation, would result in promoting the hydrolysis of alginate in aq. solns. Alginate, oxidized to a low extent (5%), degraded with a rate depending on the pH and temp. of the soln. This polymer was still capable of being ionically **crosslinked** with calcium ions to form gels, which degraded within 9 days in PBS soln. Finally, the use of these degradable alginate-derived **hydrogels** greatly improved cartilage-like tissue formation in vivo, as compared to alginate **hydrogels**.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:456938 CAPLUS
DOCUMENT NUMBER: 135:308752
TITLE: Controlled drug delivery from polymers by mechanical signals
AUTHOR(S): **Lee, Kuen Yong**; Peters, Martin C.; **Mooney, David J.**
CORPORATE SOURCE: Departments of Biol. & Mater. Sci., Chem. Eng., and Biomedical Eng., Univ. of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Advanced Materials (Weinheim, Germany) (2001), 13(11), 837-839
CODEN: ADVMEW; ISSN: 0935-9648
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was hypothesized that the interaction of drug mols. with the polymers used for controlled drug delivery might play a crit. role in mediating drug delivery in response to mech. signals. To test this hypothesis, three different model drugs were incorporated into alginate **hydrogels**, i.e., trypan blue, methylene blue, and vascular endothelial growth factor (VEGF). The effect of mech. signals on drug release from polymers was examd. using these model drugs. Mech. signals were not able to significantly alter the cumulative release of trypan blue, possibly due to the relatively rapid depletion from alginate **hydrogel** blue to its low mol. wt. and the lack of the interaction with the **hydrogel**. Due to the stronger interaction with alginate, the release rate and the overall cumulative release of methylene blue was more dependent on mech. signaling than those of trypan blue. The

release rate of VEGF under mech. signaling increased up to six times higher than that of control gels. Mech. signals can actively trigger the release of interactive drugs, e.g., peptides or proteins, from polymers in a controlled manner over time, suggesting a means to design advanced materials suitable for general drug-delivery applications and tissue engineering applications.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:430889 CAPLUS
DOCUMENT NUMBER: 135:262184
TITLE: Degradable and injectable poly(aldehyde guluronate) **hydrogels** for bone tissue engineering
AUTHOR(S): **Lee, Kuen Yong**; Alsberg, Eben; **Mooney, David J.**
CORPORATE SOURCE: Department of Biomedical Engineering, Department of Chemical Engineering, Department of Biologic & Materials Sciences, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Journal of Biomedical Materials Research (2001), 56(2), 228-233
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Degradable and injectable **hydrogels** may be ideal for bone-tissue engineering, esp. in the craniofacial region because of the ease of access for injection. Alginate **hydrogels** potentially could be used as injectable cell delivery vehicles, but they exhibit a limited range of mech. properties and uncontrollable disintegration time. Therefore we synthesized new **hydrogels**, composed of poly(aldehyde guluronate) (PAG) and adipic acid dihydrazide, that have a wide range of mech. stiffness and controllable degrdn. rate. MC3T3-E1 cells adhered and multiplied on PAG **hydrogels** in vitro. When primary rat calvarial osteoblasts were mixed with PAG **hydrogels** and s.c. injected into the backs of mice, mineralized bone tissues were formed 9 wk following implantation. These **hydrogels** may find wide utility as an injectable delivery system for bone precursor cells as well as for other applications in tissue engineering.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:390992 CAPLUS
DOCUMENT NUMBER: 135:127003
TITLE: **Hydrogels** for Tissue Engineering
AUTHOR(S): **Lee, Kuen Yong; Mooney, David J.**
CORPORATE SOURCE: Departments of Biologic & Materials Sciences Chemical Engineering and Biomedical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Chemical Reviews (Washington, D. C.) (2001), 101(7), 1869-1879
CODEN: CHREAY; ISSN: 0009-2665
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 154 refs. Design parameters for **hydrogels** in tissue engineering, **hydrogels** from natural polymers (collagen, gelatin, hyaluronate, fibrin, alginate, agarose, and chitin), **hydrogels** from synthetic polymers (polyacrylic acid and derivs., polyethylene oxide and copolymers, polyvinyl alc., polyphosphazene, and polypeptides), and future perspectives are indexed.
REFERENCE COUNT: 154 THERE ARE 154 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:204203 CAPLUS
TITLE: Effect of mechanical stimulation on growth factor release from synthetic extracellular matrices
AUTHOR(S): **Lee, Kuen Yong**; Peters, Martin C.; Anderson,

Kenneth W.; **Mooney, David J.**
CORPORATE SOURCE: Departments of Biologic & Materials Sciences and Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Abstr. Pap. - Am. Chem. Soc. (2001), 221st, PMSE-499
CODEN: ACSRAL; ISSN: 0065-7727
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB Polymeric matrixes are one crit. element in tissue engineering as they mimic roles of natural extracellular matrixes of tissues. The delivery of growth factors from these polymeric matrixes is one exciting method to regenerate tissues or organs. However, most delivery systems have been designed to operate under static conditions even though many tissues exist in a mech. dynamic environment. Therefore, we hypothesized that polymeric matrixes, releasing growth factors in response to mech. signals, could provide a novel means to engineer tissues in mech. stressed environments. We report here a model system of alginate **hydrogel** and vascular endothelial growth factor (VEGF), which can upregulate the release of the growth factor and promote blood vessel formation in response to mech. signaling. This approach may find numerous applications in tissue engineering as well as in more general drug delivery.

L8 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:522283 CAPLUS
DOCUMENT NUMBER: 133:256628
TITLE: Sustained and controlled release of daunomycin from cross-linked poly(aldehyde guluronate) **hydrogels**
AUTHOR(S): Bouhadir, Kamal H.; Kruger, Geneveive M.; **Lee, Kuen Yong**; **Mooney, David J.**
CORPORATE SOURCE: Department of Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Journal of Pharmaceutical Sciences (2000), 89(7), 910-919
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have incorporated daunomycin, an antineoplastic agent, into a biodegradable **hydrogel** through a labile covalent bond. In brief, sodium alginate was chem. broken down to low mol. wt. and followed by oxidn. to prep. poly(aldehyde guluronate). Adipic dihydrazide was used to incorporate the drug into the polymer backbone and cross-link the polymer to form **hydrogels**. Daunomycin can be released from the **hydrogel** after the hydrolysis of the covalent linkage between the drug and the polymer. A wide range of release profiles of daunomycin (e.g., from 2 days to 6 wk) has been achieved using these materials, and the biol. activity of the released daunomycin was maintained.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:334362 CAPLUS
TITLE: Decoupling the degradation behavior and mechanical properties of covalently cross-linked **hydrogels**.
AUTHOR(S): **Lee, Kuen Yong**; Bouhadir, Kamal H.; **Mooney, David J.**
CORPORATE SOURCE: Departments of Chemical Engineering, Biomedical Engineering, and Biologic & Materials Sciences, University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), POLY-182. American Chemical Society: Washington, D. C.
CODEN: 69CLAC
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB One typically desires to control the mech. and degrdn. properties of **hydrogels** used in biomedical applications. The mech. properties and degrdn. time of **hydrogels** typically increase or decrease together as the **crosslinking** d. is varied, and this can be a

limitation of these materials. We hypothesized that the mech. properties and degrdn. time of **hydrogels** could be decoupled by utilizing partially bound **crosslinking** mols. that are capable of reversibly **crosslinking** the polymer to form the **hydrogel** . We now report the decoupled degrdn. behavior and mech. properties of **hydrogels** formed by the covalent **crosslinking** of poly(aldehyde guluronate) (PAG). The degrdn. behavior generally depends on the **crosslinking** d. However, **hydrogels** with many dangling single-end mols. showed a retarded degrdn. behavior irresp. of their low initial modulus and low **crosslinking** d. This approach to control the properties of **hydrogels** may find wide utilities in drug delivery, tissue engineering, and other applications of **hydrogels**.

L8 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:334361 CAPLUS
TITLE: Controlled mechanical properties of alginate **hydrogels** by cross-linking with poly(ethylene glycol)-diamines.
AUTHOR(S): Eiselt, Petra; **Lee, Kuen Yong; Mooney, David J.**
CORPORATE SOURCE: Department of Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), POLY-181. American Chemical Society: Washington, D. C. CODEN: 69CLAC
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Alginate **hydrogels** have been attractive for a variety of biomedical applications. However, they have a limited range of mech. properties when ionically cross-linked with divalent cations. Therefore, covalent **crosslinking** of alginate with poly(ethylene glycol)-diamines was investigated as a means to generate **hydrogels** with a wide range of mech. properties. The elastic moduli of alginate **hydrogels** increased gradually with an increase in the **crosslinking** d. regardless of the mol. wt. of PEG, and then decreased. This interesting finding is attributed to the elastic properties of PEG as a second macromol. resulting in deviation from the rubber-elasticity theory. In addn., this study suggests that one can make two different **hydrogels** with same elastic modulus but with different compn. of alginate and PEG. This approach to control the mech. properties of **hydrogels** may find potential applications in the field of drug delivery and tissue engineering.

L8 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:261337 CAPLUS
DOCUMENT NUMBER: 133:94425
TITLE: Controlling Mechanical and Swelling Properties of Alginate **Hydrogels** Independently by Cross-Linker Type and Cross-Linking Density
AUTHOR(S): **Lee, Kuen Yong**; Rowley, Jon A.; Eiselt, Petra; Moy, Erick M.; Bouhadir, Kamal H.; **Mooney, David J.**
CORPORATE SOURCE: Department of Biomedical Engineering Chemical Engineering Biologic Materials Sciences and Materials Science Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Macromolecules (2000), 33(11), 4291-4294 CODEN: MAMOBX; ISSN: 0024-9297
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mech. and swelling properties of alginate **hydrogels** can be controlled by **crosslinker** type and d. Alginate **hydrogels** were covalently **crosslinked** with various mols. of different sized and structure, including adipic dihydrazide, lysine, and poly(ethylene glycol)-diamines to control the mech. and swelling properties of the **hydrogels**.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:208161 CAPLUS
DOCUMENT NUMBER: 132:348450
TITLE: Decoupling the degradation behavior and mechanical properties of covalently cross-linked **hydrogels**
AUTHOR(S): **Lee, Kuen Yong**; Bouhadir, Kamal H.; **Mooney, David J.**
CORPORATE SOURCE: Departments of Chemical Engineering Biomedical Engineering, and Biologic & Materials Sciences, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (2000), 41(1), 297-298
CODEN: ACPPAY; ISSN: 0032-3934
PUBLISHER: American Chemical Society, Division of Polymer Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Decoupling degrdn. followed by the changes of wt. loss, shear modulus, and swelling ratio was studied for sodium polyguluronate gels **crosslinked** with adipic acid dihydrazide.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:208160 CAPLUS
DOCUMENT NUMBER: 132:348449
TITLE: Controlled mechanical properties of alginate **hydrogels** by cross-linking with poly(ethylene glycol)-diamines
AUTHOR(S): Eiselt, Petra; **Lee, Kuen Yong**; **Mooney, David J.**
CORPORATE SOURCE: Department of Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (2000), 41(1), 295-296
CODEN: ACPPAY; ISSN: 0032-3934
PUBLISHER: American Chemical Society, Division of Polymer Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Covalently **crosslinked** sodium alginate **hydrogels** with controllable mech. properties are reported. Polyethylene glycol derivs. were chosen as **crosslinking** mols. because of their biocompatibility and hydrophilicity..
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:799967 CAPLUS
DOCUMENT NUMBER: 132:156673
TITLE: Degradation Behavior of Covalently **Crosslinked** Poly(aldehyde guluronate) **Hydrogels**
AUTHOR(S): **Lee, Kuen Yong**; Bouhadir, Kamal H.; **Mooney, David J.**
CORPORATE SOURCE: Departments of Chemical Engineering Biomedical Engineering and Biologic & Materials Sciences, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Macromolecules (2000), 33(1), 97-101
CODEN: MAMOBX; ISSN: 0024-9297
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is a significant need in the biomedical field for **hydrogels** with controllable mech. and degradative properties. We now report the degrdn. behavior of novel **hydrogels** formed by the **crosslinking** of poly(aldehyde guluronate) (PAG). PAG was prepd. from alginate by acid hydrolysis and oxidn. and was covalently cross-linked with adipic acid dihydrazide (AAD) to form **hydrogels**. These **hydrogels** were degradable in aq. media due to the hydrolysis of hydrazone bonds formed between the aldehyde of PAG and the hydrazide of AAD. We confirmed the degrdn. behavior of PAG

hydrogels cross-linked with different concns. of AAD by monitoring the changes of dry wt., modulus, and degree of swelling. The degrdn. behavior generally depends on the **crosslinking** d. as calcd. from the Flory-Rehner equation. However, **hydrogels** with many dangling single-end mols. showed a retarded degrdn. behavior irresp. of their low initial modulus and low degree of **crosslinking** d. We hypothesize this is due to re-**crosslinking** of dangling single-end mols. during degrdn. The mech. properties and degrdn. time of **hydrogels** typically increase or decrease together as the degree of **crosslinking** is varied. However, the findings of the current study suggest that the mech. properties and degrdn. time can be decoupled by utilizing partially bound **crosslinking** mols. that are capable of reversibly **crosslinking** the polymer to form the **hydrogel** . This approach to control the properties of **hydrogels** may find wide utility in the biomedical field and other applications of these materials.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:491483 CAPLUS
DOCUMENT NUMBER: 131:303297
TITLE: Rigidity of Two-Component **Hydrogels** Prepared from Alginate and Poly(ethylene glycol)-Diamines
AUTHOR(S): Eiselt, Petra; **Lee, Kuen Yong**; **Mooney, David J.**
CORPORATE SOURCE: Departments of Chemical Engineering Biomedical Engineering and Biologic Materials Sciences, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Macromolecules (1999), 32(17), 5561-5566
CODEN: MAMOBX; ISSN: 0024-9297
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Alginate **hydrogels** have been attractive for a variety of biomedical applications, but they possess limited mech. properties when ionically **crosslinked** with divalent cations. Therefore, covalent **crosslinking** of alginate with PEG-diamines of various mol. wts. was investigated as a means to generate **hydrogels** with a range of mech. properties. **Hydrogels** with a range of elastic moduli could be generated by controlling either the chain length of the **crosslinking** mol. or the **crosslinking** d. The elastic modulus increased gradually with an increase in **crosslinking** d. or wt. fraction of PEG in the **hydrogel** up to .apprx.27% (wt./wt.) of PEG. The change of mech. properties was interpreted in terms of mol. wt. between cross-links (Mc) according to the rubber-elasticity model, and the results of this anal. were generally consistent with the measured PEG-diamine incorporation efficiencies in this range. However, as the wt. fraction of PEG in the **hydrogels** increased above 27%, regardless of the mol. wt. of PEG, the elastic moduli decreased. This is not consistent with prediction based on the rubber-elasticity theory, and this is likely due to the fact that this model does not consider **crosslinking** with a second macromol. Importantly, the results of this study suggest that the mech. properties of **hydrogels** will be strongly affected by the properties of the **crosslinking** mol. as the Mc of **hydrogels** falls below the mol. wt. of the **crosslinking** mol.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:211301 CAPLUS
DOCUMENT NUMBER: 131:35810
TITLE: Biodegradable **hydrogels** for controlled cell and drug delivery
AUTHOR(S): Bouhadir, Kamal H.; Rowley, Jon A.; Kruger, Geneveive M.; **Lee, Kuen Yong**; **Mooney, David J.**
CORPORATE SOURCE: Departments of Biomedical Engineering, Chemical Engineering and Biologic & Materials Sciences, The University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1999), 40(1), 501-502

CODEN: ACPPAY; ISSN: 0032-3934
PUBLISHER: American Chemical Society, Division of Polymer Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polymers were prepd. from alginate and are biodegradable, capable of specific cell adhesion, and have controlled mech. properties. The polymers are useful in a variety of drug delivery and tissue engineering applications.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:146211 CAPLUS
TITLE: Biodegradable **hydrogels** for controlled cell and drug delivery
AUTHOR(S): Bouhadir, Kamal H.; Rowley, Jon A.; Kruger, Geneveive M.; **Lee, Kuen Yong; Mooney, David J.**
CORPORATE SOURCE: Departments of Biomedical Engineering, Chemical Engineering and Biologic & Materials Sciences, The University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), POLY-175. American Chemical Society: Washington, D. C.
CODEN: 67GHA6
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Alginate is an attractive biomaterial for cell and drug delivery, but cells cannot adhere to this material and its degrdn. is difficult to control. Moreover, alginate **hydrogels** have a limited range of phys. properties. We have synthesized novel polymers derived from low mol. oligosaccharides derived from alginate, and covalently cross-linked these polymers to form **hydrogels** with a range of phys. properties. These **hydrogels** contain hydrolytically labile cross-links, and the degrdn. rate can be varied from days to several months. In addn., cell adhesion peptides can be readily coupled to these materials to allow for specific cell adhesion. Initial studies indicate these **hydrogels** may be useful in drug delivery and cell transplantation applications.

L10 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:734675 CAPLUS
TITLE: Engineering growing tissues
AUTHOR(S): Alsberg, Eben; Anderson, Kenneth W.; Albeiruti, Amru; Rowley, Jon A.; **Mooney, David J.**
CORPORATE SOURCE: Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(19), 12025-12030
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Regenerating or engineering new tissues and organs may one day allow routine replacement of lost or failing tissues and organs. However, these engineered tissues must not only grow to fill a defect and integrate with the host tissue, but often they must also grow in concert with the changing needs of the body over time. We hypothesized that tissues capable of growing with time could be engineered by supplying growth stimulus signals to cells from the biomaterial used for cell transplantation. In this study, chondrocytes and osteoblasts were cotransplanted on **hydrogels** modified with an RGD-contg. peptide sequence to promote cell multiplication. New bone tissue was formed that grew in mass and cellularity by endochondral ossification in a manner similar to normal long-bone growth. Transplanted cells organized into structures that morphol. and functionally resembled growth plates. These engineered tissues could find utility in treating diseases and injuries of the growth plate, testing the effect of exptl. drugs on growth-plate function and development, and investigating the biol. of long-bone growth. Furthermore, this concept of promoting the growth of engineered tissues could find great utility in engineering numerous tissue types by way of the transplantation of a small no. of precursor cells.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:669552 CAPLUS
TITLE: Injection molding of living tissues
INVENTOR(S): Bonassar, Lawrence J.; Rowley, Jon A.; **Mooney, David J.**
PATENT ASSIGNEE(S): University of Massachusetts, USA
SOURCE: PCT Int. Appl.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002067856	A2	20020906	WO 2002-US5012	20020221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002159982	A1	20021031	US 2002-81897	20020221

PRIORITY APPLN. INFO.: US 2001-271104P P 20010223

AB The invention features methods of making living tissue constructs having a predetermined shape by providing a negative mold having a defined shape; suspending isolated tissue precursor cells in a **hydrogel** to form a liquid **hydrogel**-precursor cell composition; introducing the liquid **hydrogel**-precursor cell composition into the mold; inducing gel formation to solidify the liquid **hydrogel**-precursor cell composition to form a living tissue construct; and removing the living tissue construct from the mold after gel formation.

L10 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:594653 CAPLUS
DOCUMENT NUMBER: 137:145590
TITLE: Polymer carriers for sustained release local delivery of drugs for ablation of unwanted tissue
INVENTOR(S): Richardson, Thomas; **Mooney, David J.**
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060410	A2	20020808	WO 2002-US2420	20020130
WO 2020060410	A3	20021010		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-264713P P 20010130

AB Methods for ablation, i.e., elimination or redn., of unwanted tissue, particularly tissue which is normal to be present in the body but is unwanted for either health or cosmetic reasons are described. In particular, methods for elimination of fat tissue from the body are described. A drug which acts to eliminate the undesired tissue is provided in a carrier which is biocompatible, capable of being administered by injection, and which enables a controlled release of the drug over time. The drug with carrier is administered by injection locally in the area of the unwanted tissue, resulting in elimination of the tissue in that local area. For example, poly(lactide-co-glycolide) (PLG) microspheres contg. tumor necrosis factor-.alpha. (TNF-.alpha.) were prepd. by a double emulsion technique and lyophilized. Microspheres contg. 1 or 25 .mu.g TNF-.alpha. were suspended in sterile PBS and injected into the contralateral epididymis of rats. Following an initial burst period in the first few days, TNF-.alpha. exhibited essentially zero-order release kinetics. After about 7 wk, about 25% of TNF-.alpha. was released. The localized ablation of fat mass in vivo by the sustained delivery of TNF-.alpha. from the microspheres was obsd. Delivery of either 1 or 25 .mu.g of TNF-.alpha. resulted in a drop of regional fat pad wt. to about 85% that of the contralateral control tissue. Relatively small amts. of TNF-.alpha. (1 .mu.g) were required to produce changes in the tissue. When a larger amt. of TNF-.alpha. was injected, there was no significant change in the fat pad loss compared to the loss obtained with a smaller amt. of TNF-.alpha., indicating that the sustained release of a relatively small quantity of TNF-.alpha. can produce changes in fat pad mass. This also suggests that these is a satn. point in the process of fat ablation, indicating that the amt. of the drug administered may not be as important as providing a sustained release of a smaller amt. of drug over time.

L10 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:545752 CAPLUS
TITLE: Controlling material properties of ionically cross-linked alginate **hydrogels** by varying molecular weight distribution
AUTHOR(S): Kong, Hyun-Joon; **Mooney, David J.**
CORPORATE SOURCE: Department of Biologic & Materials Sciences, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Materials Research Society Symposium Proceedings (2002), 711(Advanced Biomaterials: Characterization, Tissue Engineering and Complexity), 227-230
CODEN: MRSPDH; ISSN: 0272-9172

PUBLISHER: Materials Research Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mech. properties of alginate **hydrogels** are crit. to their successful use in tissue engineering. We hypothesized that combining alginates of differing mol. wts. would allow one to readily control and decouple the viscosity of the pre-gel soln. from the post-gel stiffness. To test this, binary **hydrogels** were prepd. by incorporating low mol. wt. (MW) alginate (Mn .apprx. 3.3 .times. 104 g/mol) into 1 %(wt./wt.) alginate solns. composed of high MW alginate (Mn .apprx. 2.2 .times. 105 g/mol). The addn. of low MW alginate had minimal effects on the soln. viscosity, allowing high solids loading in the soln. while maintaining a workable soln. However, the increased mass loading resulted in much higher stiffness gels following ionic **crosslinking** with calcium. These data may be interpreted in relation to the microstructure of the soln. vs. **hydrogel**.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:535095 CAPLUS
TITLE: Biomaterials to spatially regulate cell fate
AUTHOR(S): Rowley, Jon A.; Sun, Zhengxin; Goldman, Daniel; **Mooney, David J.**
CORPORATE SOURCE: Cell & Tissue Technology Group, BD Technologies, Research Triangle Park, NC, 27709, USA
SOURCE: Advanced Materials (Weinheim, Germany) (2002), 14(12), 886-889
CODEN: ADVMEW; ISSN: 0935-9648
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The possibility to spatially regulate the function of cells interacting with materials by designing two distinct cell fate-directing signals into the material was studied. Skeletal muscle cells were cultured on alginate **hydrogel** substrates modified with arginine (R), glycine (G), and aspartic acid (D) (RGD)-contg. peptides to permit cell adhesion. An RGD adhesion signal was used to promote myoblast adhesion and subsequent proliferation. Controlling a sol. signal such as calcium, in combination with the immobilized RGD-growth signal, would spatially regulate skeletal muscle differentiation in vitro. Maintenance of cells in a normal concn. of calcium allowed cells to proliferate to confluence, and subsequently fuse in a uniform manner to form multinucleated muscle fibers. However, increasing calcium concn., while not inhibiting cell adhesion, fully inhibited myoblast fusion. Extremely high calcium concns. led to a loss of adhesion and viability of cells. RGD adhesive signals promotes multiplication of cells in direct contact with this signal, while the calcium gradient resulting from its release spatially regulates the ability of cells to differentiate.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:209463 CAPLUS
DOCUMENT NUMBER: 137:252907
TITLE: Alginate type and RGD density control myoblast phenotype
AUTHOR(S): Rowley, Jon A.; **Mooney, David J.**
CORPORATE SOURCE: Department of Biomedical Engineering, Colleges of Engineering and Dentistry, University of Michigan, Ann Arbor, MI, USA
SOURCE: Journal of Biomedical Materials Research (2002), 60(2), 217-223
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alginates are being increasingly used for cell encapsulation and tissue engineering applications; however, these materials cannot specifically interact with mammalian cells. We have covalently modified alginates of varying monomeric ratio with RGD-contg. cell adhesion ligands using carbodiimide chem. to initiate cell adhesion to these polymers. We

hypothesized that we could control the function of cells adherent to RGD-modified alginate **hydrogels** by varying alginate polymer type and cell adhesion ligand d., and we have addressed this possibility by studying the proliferation and differentiation of C2C12 skeletal myoblasts adherent to these materials. RGD d. on alginates of varying monomeric ratio could be controlled over several orders of magnitude, creating a range of surface densities from 1-100 fmol/cm2. Myoblast adhesion to these materials was specific to the RGD ligand, because adhesion could be competed away with sol. RGD in a dose-dependent manner. Myoblast proliferation and differentiation could be regulated by varying the alginate monomeric ratio and the d. of RGD ligands at the substrate surface, and specific combinations of alginate type and RGD d. were required to obtain efficient myoblast differentiation on these materials.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:744008 CAPLUS
DOCUMENT NUMBER: 136:406803
TITLE: In vivo characterization of a porous **hydrogel** material for use as a tissue bulking agent
AUTHOR(S): Loebsack, Anna; Greene, Kim; Wyatt, Sharon; Culberson, Cathy; Austin, Catherine; Beiler, Rudy; Roland, Wendy; Eiselt, Petra; Rowley, Jon; Burg, Karen; **Mooney, David**; Holder, Walter; Halberstadt, Craig
CORPORATE SOURCE: Department of General Surgery, Cannon Research Center, Carolinas Medical Center, Charlotte, NC, 28232-2861, USA
SOURCE: Journal of Biomedical Materials Research (2001), 57(4), 575-581
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tissue engineered biomaterial constructs are needed for plastic and reconstructive applications. To successfully form a space-filling tissue, the construct should induce a minimal inflammatory response, create minimal or no fibrotic capsule, and establish a vascular bed within the first few days after implantation to ensure survival of the implanted cells. In addn., the biomaterial should support cellular adhesion and induce tissue ingrowth. A macroporous **hydrogel** bead using sodium alginate covalently coupled with an arginine, glycine, and aspartic acid-contg. peptide was created. A 6-mo s.c. rat model study was performed to det. if the implanted material induced tissue ingrowth throughout the implantation area and maintained a three-dimensional vascular bed. The implanted materials produced a vascular bed, minimal inflammation and capsule formation, and good tissue ingrowth throughout the expt. The material retained its bulking capacity by demonstration of no significant change of the cross-sectional area as measured from the center of the implants after the 2-wk time point. In addn., the granulation tissue formed around the implant was loosely organized, and the surrounding tissue had integrated well with the implant. These results indicate that this material has the desired properties for the development of soft-tissue-engineering constructs.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:417022 CAPLUS
DOCUMENT NUMBER: 135:34553
TITLE: Reversible **crosslinked hydrogels** from oxidized **polysaccharides**
INVENTOR(S): Yong, Lee Kuen; **Mooney, David J.**
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA; Yong Lee, Kuen
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040314	A1	20010607	WO 2000-US32360	20001127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1244709	A1	20021002	EP 2000-989207	20001127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002002454	A	20020709	NO 2002-2454	20020524

PRIORITY APPLN. INFO.: US 1999-167632P A2 19991126
WO 2000-US32360 W 20001127

AB A **hydrogel** compn. and methods of prepg. and using the same are disclosed. The **hydrogel** compn. comprises an oxidized **polysaccharide**, e.g., alginate, and a **crosslinker** having at least two functional **crosslinking** groups, e.g., dihydrazide. The **crosslinker** reversibly **crosslinks** the **polysaccharide** and is provided in an amt. to provide dangling **crosslinkers**. The method of prepg. a **hydrogel** comprises the steps of providing an oxidized **polysaccharide**, and providing a **crosslinker**. The **crosslinker** is mixed with the **polysaccharide** at a concn. of the **crosslinker** sufficient to form a **hydrogel** wherein the **crosslinker** reversibly **crosslinks** the **polysaccharide** and has dangling **crosslinkers**. The **hydrogels** are useful, for example, for tissue engineering, cell transplantation and drug delivery applications.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:380374 CAPLUS
DOCUMENT NUMBER: 134:371799
TITLE: Sustained drug delivery from polymer matrixes
INVENTOR(S): **Mooney, David J.**; Shea, Lonnie D.; Peters, Martin C.; Liao, Elly; Richardson, Thomas P.
PATENT ASSIGNEE(S): Regents of the University of Michigan, USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035932	A2	20010525	WO 2000-US31754	20001117
WO 2001035932	A3	20020307		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-166191P P 19991118

AB Disclosed are pre-fabrication methods for prepg. particular 3-dimensional structural matrixes contg. proteins and/or drugs, the resultant compns. and in vitro and in vivo methods for the prolonged release of proteins and/or drugs in various biol. environments. The pre-fabrication processes provide protein- and/or drug-matrix materials with both high incorporation efficiencies and control over sustained protein and/or drug release. The resultant matrixes are thus particularly useful in vivo biodelivery embodiments, providing control over spatial delivery and differential

release kinetics of multiple biol. components. Thus, 125I-labeled vascular endothelial growth factor (VEGF) was first added to a soln. of 1% sodium alginate, and then beads of this soln. were gelled by injecting droplets into a aq. soln. contg. calcium chloride. The alginate beads were collected, rinsed, and lyophilized. The lyophilized beads were mixed with 85:15 PLGA and NaCl particles and the mixt. compression molded and processed with a gas foaming/particulate leaching process. Following salt leaching and drying, the matrixes were placed in the serum-free tissue culture medium and maintained at 37.degree.. The released growth factor was normalized to the total incorporated growth factor.

L10 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:312348 CAPLUS
DOCUMENT NUMBER: 135:157625
TITLE: Injection molding of chondrocyte/alginate constructs in the shape of facial implants
AUTHOR(S): Chang, Sophia C. N.; Rowley, Jon A.; Tobias, Geoffrey; Genes, Nicholas G.; Roy, Amit K.; **Mooney, David J.**; Vacanti, Charles A.; Bonassar, Lawrence J.
CORPORATE SOURCE: Center for Tissue Engineering, Department of Anesthesiology, University of Massachusetts Medical School, Worcester, MA, 01655, USA
SOURCE: Journal of Biomedical Materials Research (2001), 55(4), 503-511
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Over one million patients per yr undergo some type of procedure involving cartilage reconstruction. Polymer **hydrogels**, such as alginate, have been shown to be effective carriers for chondrocytes in s.c. cartilage formation. The goal of our current study was to develop a method to create complex structures (nose bridge, chin, etc.) with good dimensional tolerance to form cartilage in specific shapes. Molds of facial implants were prepd. using Silastic ERTV. Suspensions of chondrocytes in 2% alginate were gelled by mixing with CaSO4 (0.2 g/mL) and injected into the molds. Constructs of various cell concns. (10, 25, and 50 million/mL) were implanted in the dorsal aspect of nude mice and harvested at times up to 30 wk. Anal. of implanted constructs indicated progressive cartilage formation with time. Proteoglycan and collagen constructs increased with time to approx. 60% that of native tissue. Equil. modulus likewise increased with time to 15% that of normal tissue, whereas hydraulic permeability decreased to 20 times that of native tissue. Implants seeded with greater concns. of cells increased proteoglycan content and collagen content and equil. and decreased permeability. Prodn. of shaped cartilage implants by this technique presents several advantages, including good dimensional tolerance, high sample-to-sample reproducibility, and high cell viability. This system may be useful in the large-scale prodn. of precisely shaped cartilage implants.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:742172 CAPLUS
DOCUMENT NUMBER: 133:311081
TITLE: Macroporous open-pore **hydrogels** and their production
INVENTOR(S): Eiselt, Petra; Halberstadt, Craig; **Mooney, David**; Yeh, Julia; Latvala, Rachel; Rowley, Jon A.
PATENT ASSIGNEE(S): Regents of the University of Michigan, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061668	A1	20001019	WO 2000-US9466	20000410

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1169378 A1 20020109 EP 2000-921953 20000410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-128681P P 19990409
WO 2000-US9466 W 20000410

AB This invention is directed to a new approach to form porous sodium alginate **hydrogel** materials by first creating gas pockets in the gel and then removing this gas. The removal of the gas creates a porous material, and the initial incorporation of sufficient gas allows one to create a material with an open, interconnected pore structure. Advantageous features of the resulting materials, in addn. to their interconnected pore structure, may include that the pore structure is maintained over extended time periods and that the gels maintain a high mech. integrity that allows seeding with cells and implantation without destruction or compression of the material. The novelty resides in the correct ratio of surfactant (such as bovine serum albumin) to sodium bicarbonate blowing agent; calcium chloride is used to gel the alginate and acetic acid reacts with the bicarbonate to generate CO2 gas bubbles.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:327584 CAPLUS
TITLE: Localized delivery of antineoplastic agents with injectable oxidized alginate **hydrogels**.
AUTHOR(S): Bouhadir, Kamal H.; Sy, Gavin; **Mooney, David J.**
CORPORATE SOURCE: Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), BIOT-356. American Chemical Society: Washington, D. C. CODEN: 69CLAC
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB The localized delivery of antineoplastic agents is an attractive approach in treating cancer, as this may minimize the adverse side effects of these agents when administered systemically. We have developed a novel injectable and biodegradable **hydrogel** that is derived from alginate. These **hydrogels** are cross-linked with hydrolytically labile bonds and their degrdn. time can be readily controlled from one week to three months. We have designed the **hydrogels** to release drugs via three mechanisms, diffusion, chem. hydrolysis, and ionic decomplexation. Methotrexate, an antineoplastic agent, was used as a model drug for diffusion controlled release. Antibiotics from the anthracycline family have been covalently incorporated into the **hydrogel** and are released following the hydrolysis of the covalent linkage. Mitoxantrone has been incorporated into the **hydrogel** by ionic complexation and is released after the degrdn. of the **hydrogel**. These **hydrogels** show promise for the local delivery of single and combinations of antineoplastic agents.

L10 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:260076 CAPLUS
DOCUMENT NUMBER: 132:284256
TITLE: **Hydrogels** and water soluble polymeric carriers for drug delivery
INVENTOR(S): Bouhadir, Kamal H.; Kruger, Genevieve M.; **Mooney, David J.**
PATENT ASSIGNEE(S): The University of Michigan, USA
SOURCE: PCT Int. Appl., 65 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021572	A2	20000420	WO 1999-US23396	19991008
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964198	A1	20000501	AU 1999-64198	19991008
EP 1117444	A2	20010725	EP 1999-951843	19991008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527408	T2	20020827	JP 2000-575544	19991008

PRIORITY APPLN. INFO.: US 1998-103595P A2 19981009
WO 1999-US23396 W 19991008

AB Carriers for drug delivery, were prepd. and conjugated to drugs for sustained release of drug. E.g., Na alginate was hydrolyzed to give Na polyguluronate which was oxidized to aldehyde form and then **crosslinked** with adipic dihydrazide to give a **hydrogel**. Daunomycin was then conjugated with this **hydrogel**.

L10 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:736893 CAPLUS
DOCUMENT NUMBER: 131:332976
TITLE: Sustained dna delivery from structural porous matrices for gene therapy applications with special emphasis is on bone formation and regeneration
INVENTOR(S): Shea, Lonnie D.; Bonadido, Jeffrey; **Mooney, David J.**
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958656	A2	19991118	WO 1999-US10330	19990512
WO 9958656	A3	20000106		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BJ, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9938986	A1	19991129	AU 1999-38986	19990512

PRIORITY APPLN. INFO.: US 1998-85305P P 19980513
US 1998-109054P P 19981119
WO 1999-US10330 W 19990512

AB Disclosed are particular 3-dimensional structural matrixes contg. DNA and their use in the prolonged release of DNA in various biol. environments. The structural matrix is a porous polymer [PLGA]-based contg. pores formed by gas foaming involving inert gases (CO2) and leaching out of a water-sol. particulate (salt, NACL, sugar, glucose, sucrose, mannitol) when exposed to body fluids. The admixt. is compression molded into a selected size and shape prior to executing the gas foaming process. The structural matrix may also be an alginate or modified alginate matrix. This structural matrix is a biocompatible or biodegradable matrix. It may also be a lactic acid polymer, glycolic acid polymer or lactic acid/glycolic acid copolymer matrix. At least part of this matrix may be

comprised of lactic acid/glycolic acid (PLGA) copolymer matrix. The structural matrix may be modified where one side section is bonded to one cell interaction mol. such as cell adhesion mols., cell attachment peptides, proteoglycan attachment peptide sequences, proteoglycans, cell adhesion **polysaccharides**, growth factors, cell adhesion enzymes, RGD peptide, fibronectin, vitronectin, Laminin A, Laminin B1, Laminin B2, collagen 1 and thrombospondin. The DNA-matrix materials are created such that they maintain a defined space, allowing cellular migration, transfection and proliferation to occur in a controlled manner. Such DNA-contg. structural matrixes are thus particularly useful in in vivo cell transfection and gene expression in the context of gene therapy. This may encode a protein for stimulating bone progenitors or wound healing in fibroblast or in tissue or organ regeneration or transplantation or an antigen for immunity or cytotoxic or apoptosis-inducing protein or a transcription factor or elongation factor or cell cycle control protein or kinase or phosphatase or DNA repair protein or oncogene or tumor suppressor or angiogenic protein or anti-angiogenic protein or immune response stimulating protein or cell surface receptor or accessory signaling mol. or transport protein or anti-bacterial or anti-viral protein or hormone or neurotransmitter or growth factor or growth factor receptor or interferon or interleukin or chemokine or cytokine or colony stimulating factor or chemotactic factor protein of growth hormone or parathyroid hormone or PTH1-34 polypeptide or bone morphogenic protein or BMP-2A or BMP-2B or BMP-3 or BMP-4 or BMP-5 or BMP-6 or BMP-7 or BMP-8 or TGF-.alpha. or TGF-.beta.1 or TGF-.beta.2 or latent TGF.beta. binding protein or activin/inhibin protein or FGF or GMCSF or EGF or PDGF or insulin-like growth factor or leukemia inhibitory factor. This method allows for the use in gene transfer to cells within a tissue site and in manuf. of a medicament for gene therapy. Implantable medical devices comprising this gene-matrix are described. The release of nucleic acids from the matrix is controlled by diffusion. This method also applies to cancer therapy or treating viral infection.

L10 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:538727 CAPLUS
DOCUMENT NUMBER: 132:113045
TITLE: Role of synthetic extracellular matrix in development of engineered dental pulp
AUTHOR(S): Bohl, Kristyn S.; Shon, John; Rutherford, Bruce; **Mooney, David J.**
CORPORATE SOURCE: Department of Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Polymers for Tissue Engineering (1998), 299-314. Editor(s): Shoichet, Molly S.; Hubbell, Jeffrey A. VSP: Utrecht, Neth. CODEN: 68AEA8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB In cases of damaged oral tissues, traditional therapies, such as a root canal, replace the injured tissue with a synthetic material. However, while the materials currently used can offer structural replacement of the lost tissue, they are incapable of completely replacing the function of the original tissue, and often fail over time. This report describes a tissue engineering approach to dental pulp tissue replacement utilizing cultured cells seeded upon synthetic extracellular matrixes. Human pulp fibroblasts were obtained and multiplied in culture. These cells were then seeded onto three different synthetic matrixes: scaffolds fabricated from polyglycolic acid (PGA) fibers, a type I collagen **hydrogel**, and alginate in an effort to examine which matrix is most suitable for dental pulp tissue formation. In addn., methods previously developed for seeding and culturing pulp cells on PGA were optimized. Culturing cells on PGA resulted in a very high cell d. tissue with significant collagen deposition. No cell proliferation was obsd. on alginate, and the growth of cells in collagen gels after 45 days was only moderate. These studies indicate dental pulp-like tissues can be engineered, and this may provide the first step to engineering a complete tooth.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:193314 CAPLUS
DOCUMENT NUMBER: 130:353884

TITLE: Synthesis of cross-linked poly(aldehyde guluronate) **hydrogels**
AUTHOR(S): Bouhadir, Kamal H.; Hausman, Debra S.; **Mooney, David J.**
CORPORATE SOURCE: Department of Chemical Engineering, Department of Biologic and Materials Sciences, The University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Polymer (1999), 40(12), 3575-3584
CODEN: POLMAG; ISSN: 0032-3861
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alginate is an attractive material for controlled drug delivery and cell transplantation applications. However, alginate **hydrogels** are not degradable, have limited mech. properties, and lack the functional groups required for cell interaction. To address these limitations of alginate while maintaining their favorable characteristics, we have synthesized new polymers derived from sodium poly(guluronate), the portion of the alginate mol. that is responsible for its gelling behavior. Sodium poly(guluronate) was isolated, oxidized with sodium periodate, and **crosslinked** with adipic dihydrazide to yield **hydrogels** with a wide range of mech. properties, and with cell adhesion peptides coupled to their backbones.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:159891 CAPLUS
DOCUMENT NUMBER: 130:342815
TITLE: Synthetic extracellular matrixes to guide tissue formation
AUTHOR(S): Peters, Martin C.; **Mooney, David J.**
CORPORATE SOURCE: Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI, 48109-1078, USA
SOURCE: International Congress Series (1998), 1170(Tissue Engineering for Therapeutic Use 2), 55-65
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 44 refs. Tissues engineered from cultured cells may potentially be utilized to treat a variety of diseases, but techniques to promote the development of proper tissue structure and function must first be developed. The native extracellular matrix (ECM) of tissues aids this process during development by providing mech. support to the forming tissue, localizing cells to specific locations, and regulating gene expression. Many investigators are attempting to create synthetic analogs to the ECM that will serve these functions, and promote new tissue formation from cultured cells. We propose to utilize combinations of macrostructures to provide tissue-level control of structure with **hydrogels** to provide cell-level guidance over cell function. Highly porous fiber-based and sponge-based macrostructures have been formed from biodegradable synthetic polymers, e.g., polyglycolic acid, using a variety of polymer processing methods. Proper design leads to synthetic ECM which provide mech. support for the developing tissue, and guidance for the development of gross tissue structure. In addn., sol. chem. signals, e.g., protein growth factors, can be delivered to cells utilizing these matrixes. We are also currently developing **hydrogels** in which cells within the macrostructures can be immobilized. These matrixes are in intimate contact with the cells and provide guidance, at the cell level, over tissue structure and function. Alginates (**polysaccharides** derived from seaweed) have been covalently modified to allow specific cellular recognition and adhesion. These synthetic ECM have shown promise to engineer a variety of tissues, including smooth muscle and dental pulp.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:767609 CAPLUS
DOCUMENT NUMBER: 130:114973
TITLE: PEG **crosslinked** alginate **hydrogels**

with controlled mechanical properties
AUTHOR(S): Eiselt, Petra; Rowley, Jon A.; **Mooney, David J.**
CORPORATE SOURCE: Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI, 48109-2136, USA
SOURCE: Materials Research Society Symposium Proceedings (1998), 530(Biomaterials Regulating Cell Function and Tissue Development), 37-42
CODEN: MRSPDH; ISSN: 0272-9172
PUBLISHER: Materials Research Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reconstruction of tissues and organs utilizing cell transplantation offers an attractive approach for the treatment of patients suffering from organ failure or loss. Highly porous synthetic materials are often used to mimic the function of the extracellular matrix (ECM) in tissue engineering, and serve as a cell delivery vehicle for the formation of tissues in vivo. Alginate, a linear copolysaccharide composed of D-mannuronic acid (M) and L-guluronic acid (G) units is widely used as a cell transplantation matrix. Alginate is considered to be biocompatible, and **hydrogels** are formed in the presence of divalent cations such as Ca2+, Ba2+ and Sr+. However, ionically **crosslinked** alginate gels continuously lose their mech. properties over time with uncontrollable degrdn. behavior. We have modified alginate via covalent coupling of **crosslinking** mols. to expand and stabilize the mech. property ranges of these gels. Several diamino PEG mols. of varying mol. wt. (200, 400, 1000, 3400) were synthesized utilizing carbodiimide chem. Sodium alginate was covalently **crosslinked** with these **crosslinking** mols., and mech. properties of the resulting **hydrogels** were detd. The elastic modulus of the **crosslinked** alginates depended on the mol. wt. of the **crosslinking** mols., and ranged from 10-110 kPa. The theor. **crosslink** d. in the **hydrogels** was also varied from 3 to 47% (relative to the carboxylic groups in the alginate) and the mech. properties were measured. The elastic modulus increased gradually and reached a max. at a cross-link d. of 15%. In summary, covalently coupled **hydrogels** can be synthesized which exhibit a wide range of mech. properties, and these materials may be useful in a no. of tissue engineering applications.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:460333 CAPLUS
DOCUMENT NUMBER: 129:217845
TITLE: A study on the permanent set of wool fabric by utilizing natural protein polymers (I) -adsorption behavior of hydrolyzed wool keratins onto wool fabrics-
AUTHOR(S): Hwang, Mun Seb; Park, Yun Heum; Jeon, Boong, Soo; Park, Chong Rae; **Lee, Kuen Yong**; Lee, Myung Hack; Park, Heung Su; Cho, Yong Ju
CORPORATE SOURCE: Department Textile Engineering, Sung Kyun Kwan University, Suwon, S. Korea
SOURCE: Han'guk Somyu Konghakhoechi (1998), 35(5), 314-320
CODEN: HSKCDQ; ISSN: 1225-1089
PUBLISHER: Korean Fiber Society
DOCUMENT TYPE: Journal
LANGUAGE: Korean
AB Adsorption behavior of hydrolyzed wool keratins onto wool fabric was studied systematically for the purpose of improving the permanent set of the fabric. The adsorption isotherm of the keratin onto the fabric was of a Langmuir type and was found to be influenced by pretreatments such as swelling and redn. of the wool. After redn., the diffusion coeff. of the hydrolyzed keratin was about 10 times as large as that of the untreated wool fabric. It was indicated from soly. and washing tests that new **crosslinks** were possibly formed by the adsorption of keratin and the subsequent oxidn. Dyeing behavior of the keratin-adsorbed wool fabric was also discussed in terms of the adsorbed amt. of hydrolyzed keratin.

L10 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:458146 CAPLUS

DOCUMENT NUMBER: 129:153196
TITLE: Role of synthetic extracellular matrix in development of engineered dental pulp
AUTHOR(S): Bohl, Kristyn S.; Shon, John; Rutherford, Bruce; **Mooney, David J.**
CORPORATE SOURCE: Department of Chemical Engineering, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Journal of Biomaterials Science, Polymer Edition (1998), 9(7), 749-764
CODEN: JBSEEA; ISSN: 0920-5063
PUBLISHER: VSP BV
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In cases of damaged oral tissues, traditional therapies, such as a root canal, replace the injured tissue with a synthetic material. However, while the materials currently used can offer structural replacement of the lost tissue, they are incapable of completely replacing the function of the original tissue, and often fail over time. This report describes a tissue engineering approach to dental pulp tissue replacement utilizing cultured cells seeded upon synthetic extracellular matrixes. Human pulp fibroblasts were obtained and multiplied in culture. These cells were then seeded onto 3 different synthetic matrixes: scaffolds fabricated from polyglycolic acid (PGA) fibers, a type I collagen **hydrogel**, and alginate in an effort to examine which matrix is most suitable for dental pulp tissue formation. In addn., methods previously developed for seeding and culturing pulp cells on PGA were optimized. Culturing cells on PGA resulted in a very high cell d. tissue with significant collagen deposition. No cell proliferation was obsd. on alginate, and the growth of cells in collagen gels after 45 days was only moderate. These indicate dental pulp-like tissues can be engineered, and this may provide the first step to engineering a complete tooth.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:328783 CAPLUS
DOCUMENT NUMBER: 129:126952
TITLE: In vitro and in vivo models for the reconstruction of intercellular signaling
AUTHOR(S): Bouhadir, Kamal H.; **Mooney, David J.**
CORPORATE SOURCE: Departments of Chemical Engineering and Biological and Materials Sciences, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Annals of the New York Academy of Sciences (1998), 842(Salivary Gland Biogenesis and Function), 188-194
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 27 refs. A crit. need in both tissue-engineering applications and basic cell culture studies is the development of synthetic extracellular matrixes (ECMs) and exptl. systems that reconstitute three-dimensional cell-cell interactions and control tissue formation in vitro and in vivo. We have fabricated synthetic ECMs in the form of fiber-based fabrics, highly porous sponges, and **hydrogels** from biodegradable polymers (e.g., polyglycolic acid) and tested their ability to regulate tissue formation. Both cell seeding onto these synthetic ECMs and subsequent culture conditions can be varied to control initial cell-cell interactions and subsequent cell growth and tissue development. Three-dimensional tissues composed of cells of interest, matrix produced by these cells, and the synthetic ECM (until it degrades) can be created with these systems. For example, smooth muscle cells can be grown on polyglycolic acid fiber-based synthetic ECMs to produce tissues with cell densities in excess of 108 cells/mL. These tissues contain extensive elastin and collagen, and the smooth muscle cells within the tissue express the contractile phenotype (e.g., .alpha.-actin staining). Similar approaches can be used to grow a no. of other tissues (e.g., dental pulp) that resemble the native tissue. These engineered tissues may provide novel exptl. systems to study the role of three-dimensional intercellular signaling in tissue development and may also find clin. application as replacements to lost or damaged tissues.

L10 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:282821 CAPLUS
DOCUMENT NUMBER: 128:283001
TITLE: Physicochemical Characteristics of Self-Aggregates of Hydrophobically Modified Chitosans
AUTHOR(S): **Lee, Kuen Yong**; Jo, Won Ho; Kwon, Ick Chan; Kim, Yong-Hee; Jeong, Seo Young
CORPORATE SOURCE: Department of Fiber and Polymer Science, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Langmuir (1998), 14(9), 2329-2332
CODEN: LANGD5; ISSN: 0743-7463
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chitosan derivs. contg. 2.8-5.1 deoxycholic acid groups per 100 anhydroglucose units of chitosan were synthesized by an EDC-mediated coupling reaction. Physicochem. properties of self-aggregates of the hydrophobically modified chitosans in aq. media were studied by the dynamic light scattering method and fluorescence spectroscopy. The mean diam. (dH) of DC4.2 self-aggregates in phosphate-buffered saline (PBS) soln. (pH 7.2) was 159 nm with unimodal size distribution (variance = 0.082). It seemed that the interparticle interaction between self-aggregates was almost negligible. The mean diam. decreased with increasing degree of substitution (DS), pH, or ionic strength of the medium. The crit. aggregation concn. (cac) of self-aggregates was detd. from the fluorescence emission spectra of pyrene. The cac value of DC4.2 in PBS soln. (pH 7.2) was 2.6 .times. 10-2 mg/mL. The cac values decreased with increasing DS, pH, or ionic strength of the medium.

L10 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:197533 CAPLUS
DOCUMENT NUMBER: 128:258671
TITLE: Materials containing **polysaccharide** chains, particularly alginates or modified alginate chains
INVENTOR(S): **Mooney, David J.**; Bouhadir, Kamal H.; Wong, Wai Hung; Rowley, Jon A.
PATENT ASSIGNEE(S): Regents of the University of Michigan, USA; Mooney, David J.; Bouhadir, Kamal H.; Wong, Wai Hung; Rowley, Jon A.
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9812228	A1	19980326	WO 1997-US16890	19970919
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9744930	A1	19980414	AU 1997-44930	19970919
AU 733716	B2	20010524		
EP 927196	A1	19990707	EP 1997-943460	19970919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001524136	T2	20011127	JP 1998-514973	19970919

PRIORITY APPLN. INFO.: US 1996-26362P P 19960919
US 1996-26467P P 19960919
US 1997-41565P P 19970321
WO 1997-US16890 W 19970919

AB The title materials comprise **polysaccharide** chains which may be included as side chains or auxiliary chains from a backbone polymer chain, which may also be a **polysaccharide**. The **polysaccharide** , e.g., alginate chains may be **crosslinked** between side chains, auxiliary chains and/or backbone chains. These materials and nonmodified

alginate materials are advantageously modified by covalent bonding of a biol. active mol. for cell adhesion or other cellular interaction. Processes for prepn. of these alginate materials and methods for using them, particularly as polymeric matrixes, e.g., for cell transplantation and tissue engineering applications are also claimed.

L10 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:160625 CAPLUS
TITLE: Covalently modified alginate.
AUTHOR(S): Rowley, Jon; Yue, Isaac; Bouhadir, Kamal; **Mooney, David**
CORPORATE SOURCE: Dept. Biomedical, University Michigan, Ann Arbor, MI, 48109-1078, USA
SOURCE: Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), COLL-390. American Chemical Society: Washington, D. C.
CODEN: 64AOAA
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB **Hydrogels** are widely used for applications in cell immobilization, cell transplantation, and in-vitro cell culture. Alginate is a natural **polysaccharide** that forms stable **hydrogels** in the presence of divalent cations. Alginate has many desirable characteristics including low diffusional resistance to nutrients, mild gelling conditions for cell immobilization, and favorable biocompatibility. However, alginate has a limited range of mech. properties and lacks adhesion ligands necessary for cell survival. Carbodiimide chem. is being applied to alginate to engineer the phys. and biol. properties for diverse applications. Variable lysine concns. are used to **crosslink** the **polysaccharide**, resulting in a range of mech. properties and shape memory. In addn., cell adhesion peptides contg. the RGD (arginine, glycine, aspartic acid) sequence have been incorporated onto alginate with subsequent enhancement of cell and tissue interactions. Therefore, covalently modifying alginate allows for the control of both mech. and biol. properties of the cell environment.

L10 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:8491 CAPLUS
DOCUMENT NUMBER: 126:135552
TITLE: Polyelectrolyte complexes of sodium alginate with chitosan or its derivatives for microcapsules
AUTHOR(S): **Lee, Kuen Young**; Park, Won Ho; Ha, Wan Shik
CORPORATE SOURCE: Dep. Fiber Polymer Sci., Seoul Natl. Univ., Seoul, 151-742, S. Korea
SOURCE: Journal of Applied Polymer Science (1997), 63(4), 425-432
CODEN: JAPNAB; ISSN: 0021-8995
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chitosan, a cationic **polysaccharide**, was heterogeneously deacetylated with a 47% sodium hydroxide soln. and followed by a homogeneous reacetylation with acetic anhydrides to control the N-acetyl content of the chitosan having a similar mol. wt. The chitosans having different degrees of N-acetylation were complexed with sodium alginate, an anionic **polysaccharide**, and the formation behavior of polyelectrolyte complexes (PECs) was examd. by the viscometry in various pH ranges. The max. mixing ratio (Rmax) increased with a decrease in the degree of N-acetylation of the chitosan at the same pH, and with a decrease in pH at the same degree of N-acetylation. Similarly, N-acylated chitosans were also prepd. The N-acyl chitosans scarcely affected the formation behavior of PECs with sodium alginates. For the application of the PECs produced, the microencapsulation of a drug was performed and the release property of drug was tested. The microcapsules were prepd. in one step by the extrusion of a soln. of guaifenesin and sodium alginate into a soln. contg. calcium chloride and chitosan through interpolymeric ionic interactions. The drug release during the drug-loaded microcapsules storage in saline was found to depend on the pH where the microcapsules were formed and the kind of N-acyl groups introduced to the chitosan.

L10 ANSWER 26 OF 26 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:485790 CAPLUS

DOCUMENT NUMBER: 125:123807
TITLE: Localized delivery of factors enhancing survival of transplanted cells
INVENTOR(S): **Mooney, David J.**; Langer, Robert S.; Vacanti, Joseph P.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA; Children's Medical Center Corporation
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9618411	A1	19960620	WO 1995-US16356	19951214
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6281015	B1	20010828	US 1994-358235	19941216
CA 2207286	AA	19960620	CA 1995-2207286	19951214
EP 794790	A1	19970917	EP 1995-943823	19951214
EP 794790	B1	20020417		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10510816	T2	19981020	JP 1995-519275	19951214
AT 216255	E	20020515	AT 1995-943823	19951214

PRIORITY APPLN. INFO.: US 1994-358235 A 19941216
WO 1995-US16356 W 19951214

AB Growth factors and/or angiogenic factors are administered in combination with dissocd. cells to be transplanted, preferably in microspheres with the cells on or in a polymeric matrix, to enhance survival and proliferation of the transplanted cells. Examples demonstrate that epidermal growth factor (EGF) was incorporated into microspheres fabricated from a copolymer of lactic and glycolic acid using a double emulsion technique, the incorporated EGF was steadily released over one month in vitro, and it remained biol. active, as detd. by its ability to stimulate DNA synthesis, division, and long-term survival of cultured hepatocytes. EGF-contg. microspheres were mixed with a suspension of hepatocytes, seeded onto porous sponges, and implanted into the mesentery of two groups of Lewis rats, to demonstrate efficacy in vivo. Two weeks after implantation in animals, devices which included EGF-contg. microspheres showed a two-fold increase in the no. of engrafted hepatocytes, as compared to implants which received blank microspheres.